Children’s Hospital of Pittsburgh
Continuity Clinic Curriculum

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Topic: Growth: Short Stature

Learning Objectives: After completing these materials, viewers will be able to:

1. Define short stature
2. Develop a differential diagnosis for short stature
3. Distinguish between pathologic and “healthy” causes of short stature
4. Outline a diagnostic and therapeutic approach to short stature

[Original module by Dr. Rajakumar, January 2005; Revised December 2007; November 2013, December 2016]

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Case 1

You are seeing CJ, a 6 year-old girl, for her annual well child check. Her parents are concerned about her short stature. Her height velocity has decelerated in the past 3 years. She was at the 50th percentile for height and weight at birth. Her weight is 20 kg (50th percentile), height is 95 cm (< 3rd percentile), and BMI is 22 (> 97th percentile).

Click here to see weight and height chart

Question 1. How do you define short stature and what constitutes growth failure?
Question 1. How do you define short stature and what constitutes growth failure?

**Definition of short stature** [adapted from: Reference 5]

- Height < 3rd percentile (*height less than 2 SDs for age and gender*)
- Projected height significantly below genetic potential (*projected adult height based on current height velocity is less than 2 SDs of the estimated mid-parental height*)

**Growth failure (Slow growth or failure to grow)**

Growth failure, as a concept, is linked to growth velocity. Growth velocity is the change of height over a period of time. Assessment of growth velocity should be based on measurements obtained over a decent interval of time (i.e. at least 6 months). Abnormally slow height velocity (rate of height gain) for chronological age constitutes growth failure.

- Abnormally slow height velocity (<2 inches or 5 cm/yr from age 3 years to puberty)
- Downward crossing of percentile track on growth chart after 18 months

Growth Hormone Research Society (GHRS) recommends for children who are 2 years or older further evaluation of children with short stature (height below 2 SD) if their height velocity over 1 year is less than 1 SD below the mean for chronological age OR if there is a decrease in height velocity of more than 0.5 SD over 1 year.

In the absence of short stature, GHRS recommends further evaluation of children with faltering height velocity, if their height velocity is more than 2 SD below the mean over 1 year or 1.5 SD sustained over 2 yrs.


For those of you who use Children’s Hospital of Pittsburgh’s electronic medical record for outpatient care, Height Velocity Charts are available on EPIC, under GROWTH CHART; Reference Data Sets.

[Click here to view an example](#)

Question 2. How do you interpret CJ’s current growth status?
Question 2. How do you interpret CJ’s current growth status?

Consider typical height velocities:

- Typical length at birth is 50 cm
- 25 cm - first year
- 12 cm - second year
- 8 cm - third year
- 5 to 6.5 cm/yr - 4 years of age until puberty

Hence the average height of a healthy 6-year-old girl is 115 cm.

CJ was at the 50th percentile for weight and length at birth. Her weight now is at the 50th percentile, but her height (95 cm) is significantly below the 3rd percentile for her age. Her growth tempo has decelerated in the past 3 years. CJ’s current growth parameters suggest a relative sparing of weight velocity with an impaired height velocity.

Question 3. What additional information you will find helpful in ascertaining the etiology of CJ’s short stature?
Question 3. What additional information you will find helpful in ascertaining the etiology of CJ’s short stature?

History
A thorough history, focusing on family growth history and relevant review of systems, is essential in the evaluation of short stature, as a variety of systemic illnesses can affect a child’s growth.

A. Family growth history:
  - Parents’ height
  - Parents’ ages of pubertal onset
  - Family history of short stature
    - Men: <5 feet 4 inches (160 cm)
    - Women: <4 feet 11 inches (150 cm)
  - Family history of delayed growth or puberty
    - Growth after high school
    - Pubertal delay in boys:
      - Absence of pubic hair or testicular enlargement by 14 yrs
      - Start shaving at 19 years or older
    - Pubertal delay in girls:
      - Breast development not started by 13 yrs
      - Menarche at 14 yrs or older
  - Family history of endocrine dysfunction or systemic causes of growth failure

B. Child’s history: When did the growth failure begin?

1. Perinatal history:
  - Antenatal & natal events
  - Birth weight
  - Potential clues during the newborn period:
    - Prolonged jaundice, hypoglycemia, micropenis
      - Hypopituitarism
    - Lymphedema:
      - Turner syndrome
Hypotonia:

- Prader-Willi syndrome
- Down syndrome

2. Growth velocity through infancy and childhood

C. Review of systems:

- Headaches
- Visual difficulties
- Recurrent infections
- Chronic cough
- Abdominal pain
- Fever
- Chronic diarrhea
- Recurrent bloody stools
- Joint pain
- Vomiting
- Constipation
- Temperature instability
- Polyuria
- Polyphagia
- Polydipsia

D. Psychosocial history

Assess for signs of:
- Abuse
- Neglect
- Emotional deprivation
- Poor parenting

Psychosocial dwarfism can be associated with:
- Primitive speech
- Social withdrawal
- Bizarre eating or drinking habits (drinking out of toilets)

E. Medication history

- Assess use of prescription and non-prescription medications and food supplements. Long-term use of steroids, stimulants, anticonvulsants and antidepressants can impair growth.
Based on the history and review of systems, a targeted physical examination would be warranted. Furthermore, if history and physical exam are not suggestive of a diagnosis, screening laboratory testing would be indicated.

Case 1 (continued)

CJ was born at term after an uncomplicated pregnancy and delivery. She is developmentally appropriate for her age. Her height velocity began to falter around three years of age. There was no family history of short stature. Her father is 180 cm (71 inches) and mother is 175 cm (69 inches) tall. Her review of systems was negative. On exam - CJ was a proportionately short, pleasant, plump, well-nourished, non-dysmorphic child without any focal findings.

Question 4. What is the most likely cause of CJ’s short stature?
Question 4. What is the most likely cause of CJ’s short stature?

CJ has short stature with normal weight velocity. Endocrine dysfunction is the most likely etiology of proportionate short stature with increased weight to height ratio. (Conversely, impaired weight velocity with spared height velocity is typical of nutritional deficiency or failure to thrive.)

- Most likely cause: **Growth hormone deficiency**
- Other possible diagnoses: **Hypothyroidism & Cushing syndrome**

Question 5. How do you evaluate CJ’s short stature?
Question 5. How do you evaluate CJ’s short stature?

Recommended lab evaluation:
- Bone age
- Thyroid function tests: Serum T<sub>4</sub> and Serum TSH
- Insulin-like growth factor 1 (IGF-I) and Insulin like growth factor binding protein-3 (IGFBP-3)

Case 1 (continued)

CJ’s bone age was markedly delayed (4 years) and her thyroid function tests were normal. IGF-1 and IGFBP-3 were low.

Question 6. How do you interpret CJ’s lab results? What are your next steps for this patient?
Question 6. How do you interpret CJ’s lab results? What are your next steps for this patient?

Low levels of IGF-1 and IGFBP-3 suggest growth hormone deficiency.

Next steps:
- Referral to endocrinology for provocative testing (Arginine, Clonidine, Levodopa, Insulin or Glucagon) to confirm the diagnosis
- Pituitary MRI: to exclude structural lesions causing growth hormone deficiency

Case 2

You are seeing RJ, a 10-year-old boy for his well child exam. His parents are concerned that he is short. His weight is 24 kg (3rd percentile) and his height is 127 cm (just below the 3rd percentile). His BMI is 14.9 (13th percentile). Plotting his height and weight show that his growth velocity for both parameters have been adequate as he has been tracking along the same percentile for height and weight since 3 years of age.

Click here to see the Case 2 weight and height chart

Question 7. How do you interpret RJ’s growth curve?
Question 7. How do you interpret RJ’s growth curve?

RJ has short stature by definition (height below 3rd percentile). However, his height velocity and weight velocity have been adequate since infancy. It is likely that RJ has one of 2 possible normal variants of short stature:

- Constitutional delay in growth and puberty
  or
- Familial (genetic) short stature

Question 8. What additional history would be helpful?
**Question 8. What additional history would be helpful?**

Family growth history would be most helpful in ascertaining the likely cause of RJ’s short stature.

Review of systems is also important; to ensure that there is no underlying systemic etiology or endocrine etiology.

**Scenario 1**

RJ is an only child. His parents are healthy and deny any family history of short stature. His father remembers being relatively short in his class until the onset of puberty (at 15 years). However, after the onset of puberty, he started to grow, and did not stop growing until freshman year of college. His present height is 175 cm (70 inches). RJ’s mother was of average height during childhood and attained menarche at 12 years of age. Now she is 165 cm (66 inches) tall.

RJ denies any symptoms suggestive of endocrinopathy or systemic illness. He has a normal appetite and has been eating a balanced, nutritionally adequate diet. He is pre-pubertal and has a non-focal physical exam.

**Question 9. How do you interpret RJ’s parental heights? Can you predict RJ’s final height based on his parental height?**
Question 9. How do you interpret RJ’s parental heights? Can you predict RJ’s final height based on his parental height?

RJ's parental heights are normal. Mid-parental height would predict RJ’s adult height based on his genetic potential. The formula for mid-parental height is:

For boys:  \[
\frac{\text{Father's height (cm)} + \text{Mother's height (cm)} + 13}{2}
\]
\[
\frac{\text{Father's height (inches)} + \text{Mother's height (inches)} + 5}{2}
\]

For girls:  \[
\frac{\text{Father's height (cm)} + \text{Mother's height (cm)} - 13}{2}
\]
\[
\frac{\text{Father's height (inches)} + \text{Mother's height (inches)} - 5}{2}
\]

RJ’s mid-parental height:  \[
\frac{175 + 165 + 13}{2} = 176.5 \text{ cm}
\]

The expected adult height typically falls within ± 8.5 cm of the mid-parental height.

RJ’s expected adult height would fall between 168 cm (3rd percentile) and 185 cm (97th percentile).

As the 95% prediction interval of the mid-parental height is large, it's often clinically not helpful.

Mid-parental Height Usefulness and Caveats (References 15 & 17)

Marked deviation of the projected growth trajectory from mid-parental height could imply underlying pathological causes of short stature. However, such predictions are often invalid, if parental heights are far apart or if they had been affected by growth altering conditions during their childhood.

However, in variations of normal growth or pathological short stature, the projected adult height, determined by projecting the child’s growth along the current height percentile to the 20-year point on the growth chart, varies by more the 5 CM from the mid-parental height.

- RJ’s projected adult height = 164 CM
- Mid-parental Height = 176.5 cm

Click here to see the RJ Case 2 weight and height chart

Based on the family history of delayed onset of growth tempo and puberty in dad, RJ most likely has constitutional delay in growth and puberty - a normal variation of growth pattern.
Question 10. What test would confirm this diagnosis?

Obtain a bone age based on x-ray of the left wrist using Greulish and Pyle’s radiographic atlas of skeletal development.

Bone age is delayed relative to chronological age in constitutional delay in growth and puberty.

Question 11. How do you counsel RJ’s family?
**Question 11. How do you counsel RJ’s family?**

RJ’s family can be reassured that RJ has a normal variation in growth pattern and that his final adult height will be in the normal range.

**Constitutional delay in growth and puberty** (“late bloomers”):

- Linear growth slows during the first three years (downward crossing of height & weight percentiles)
- Height velocity remains normal but parallel to just below the 5th percentile during the prepubertal period
- Delayed skeletal age (bone age) and pubertal onset
- Family history of parents being short during childhood and having had late pubertal growth spurt, with normal adult heights
- Besides delayed bone age, all other laboratory tests are normal
- Final adult height is normal and usually within the predicted target range

**Scenario 2**

RJ is an only child. His parents are healthy but short. His dad is 165 cm (66 inches) tall and his mom is 152 cm (60.8 inches) tall.

RJ denies any symptoms suggestive of endocrinopathy or systemic illness. He has a normal appetite and has been eating a balanced, nutritionally adequate diet. He is pre-pubertal and has a non-focal physical exam.

**Question 12. How do you interpret RJ’s parental heights? Can you predict RJ’s final height based on his parental height?**
Question 12. How do you interpret RJ’s parental heights? Can you predict RJ’s final height based on his parental height?

RJ’s parents are relatively short. His mid-parental height is:

\[(165 + 152 + 13) ÷ 2 = 165 \text{ cm}.\]

The expected adult height typically falls within ± 8.5 cm of the mid-parental height.

Therefore, RJ’s expected adult height would fall between 156.5 cm (3rd percentile) to 173.5 cm (97th percentile).

As RJ’s projected adult height (164 cm), determined by projecting his current height percentile to the 20-year point on the growth chart, falls within 10 cm of the mid-parental height (165 cm), his current height can be deemed as appropriate for his familial growth potential.

Click here to see the weight and height chart

RJ has familial short stature.

Question 13. What additional test would help to distinguish familial short stature from constitutional growth delay?
Question 13. What additional test would help to distinguish familial short stature from constitutional growth delay?

Obtain a bone age.

**Bone age is the same as chronological age in familial short stature** (in contrast to delayed bone age in constitutional delay in growth and puberty).

Question 14. How do you counsel RJ and his family in this scenario?
Question 14. How do you counsel RJ and his family in this scenario?

RJ has familial (genetic) short stature. His adult height will be short, but consistent with his genetic growth potential and will fall within the projected target height based on the mid-parental height.

Familial short stature (FSS)

- Children with FSS tend to be of normal weight and length at birth
- Their height velocity tracks downwards towards a percentile track consistent with their genetic growth potential by 2 years of age
- They track a short growth channel (below 3rd percentile), with normal or near normal velocity
- Laboratory tests are all normal, including bone age
- Final adult height is short but consistent with mid-parental target height

Familial short stature falls under the diagnostic umbrella of “idiopathic short stature (ISS)”, i.e., short stature without a known etiology.

Question 15. RJ’s parents ask you if growth hormone injections would accelerate his height velocity and help him exceed his current predicted adult height?
Question 15. RJ’s parents ask you if growth hormone injections would accelerate his height velocity and help him exceed his current predicted adult height?

Usage of growth hormone in the treatment of idiopathic short stature has been contentious and controversial. FDA approved the use of recombinant human growth hormone for the treatment of idiopathic short stature in May 2003. However, one ought to consider the pros and cons of growth hormone therapy before embarking on it for an apparently normal child (a child without growth hormone deficiency or obvious pathologic cause for growth failure). Consultation with a child psychologist/psychiatrist might help the family and child cope with the anxiety and social issues associated with short stature. In the event the family is still seeking growth hormone therapy, a pediatric endocrinologist should be consulted.

Pros and cons of growth hormone therapy

Pros:
- Randomized controlled trials have shown that growth hormone augment the final adult height, even though the increase is small (4 to 6 cm)
- Treatment could help allay parental/patient anxiety

Cons:
- Ethical concerns: Are we treating a normal state?
- Long-term treatment risk-benefit unknown
- Common side effects:
  - Joint pain
  - Edema
  - Bruising
  - Local reactions
- Less common side effects:
  - Pseudotumor cerebri
  - Slipped capital femoral epiphysis
  - Gynecomastia
  - Glucose intolerance
  - Progression of scoliosis
- Costs
  - Estimated cost $35,000-$50,000 per inch of gain in adult height
Take Home Points

*Indications for Referral to a Pediatric Endocrinologist or further work-up in Children with Short Stature*

- Children with intrauterine growth retardation who do not catch up to their growth curve by 2 years of age
- Height <3 SDs of the mean height for age
- Growth velocity <5 cm (2 in)/year in prepubertal children who are 4 yr of age or older.
- No onset of puberty by 14 years of age in boys or 13 years of age in girls
- Projected height <2 SDs of the mid-parental height or projected height that’s below the mid-parental height by more than 5 CM
- Bone age <2 SDs of the chronologic age
- Diagnosis of conditions approved for recombinant growth hormone therapy
Etiologic and diagnostic approach to short stature

References:


